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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/822,787 | 04/13/2004 | Jian Ni | PF221D2 | 3664 |

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HUMAN GENOME SCIENCES INC.
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| EXAMINER | |
|---|---|
| O HARA, EILEEN B | |
| ART UNIT | PAPER NUMBER |
| 1646 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 01/12/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/822,787 | NI ET AL. | |
| | Examiner | Art Unit | |
| | Eileen B. O'Hara | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-32 are pending in the instant application.

### *Information Disclosure Statement*

2. The information disclosure statement (IDS) submitted on April 13, 2004 was has been considered by the examiner.

### *Priority*

3. Applicant is reminded of the following requirement:

In a continuation or divisional application (other than a continued prosecution application filed under 37 CFR 1.53(d)), the first sentence of the specification or application data sheet (37 CFR 1.76) should include a reference to the prior application(s) from which benefit of priority is claimed, and also the status. See 37 CFR 1.78. Application 09/971,187, now U.S. Patent 6,746,674, should be included.

### *Specification*

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Antibodies to Cytostatin II.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 5-8, 23 and 27-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The enablement of the claims requires the cDNA accorded ATCC Deposit No. 97287. Applicants' referral to the deposit of human cytostatin II cDNA as accession number 97287 on page 17 of the specification is an insufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met. If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Additionally, amendment of the specification to recite the date of the deposit is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6.1 Claims 1-9 and 12-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over R. Godbout, Experimental Eye Research, Vol. 56, Issue 1, January 1993, pages 95-106, further in view of Immunobiology, The Immune System in Health and Disease, Third Edition, Janeway and Travers, Ed., 1997.

Claims 1-9 and 12-32 are directed to isolated antibody or fragment thereof that specifically binds to a protein consisting of amino acid residues 1-132 of SEQ ID NO: 2, or 30 or 50 consecutive amino acids of SEQ ID NO: 2, or full-length or fragment of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 97287 or 30 or 50 consecutive amino acids thereof, wherein the antibody is human, polyclonal, monoclonal, chimeric or humanized or single chain or Fab fragment, or labeled, in which the label is an enzyme,

fluorescent, luminescent, or bioluminescent, binds specifically to said protein in a Western blot or ELISA, isolated cell that produces the antibody or fragment thereof, hybridoma that produces the antibody or fragment thereof, method of detecting the polypeptide in a biological sample comprising contacting the biological sample with the antibody or fragment thereof, wherein the antibody or fragment thereof was obtained from an animal that has been immunized with the polypeptide.

Godbout discloses two proteins, one of which is 93% identical and another 92% identical to the protein of SEQ ID NO: 2 of the instant application, and which are apparently species orthologs (chicken) to the human protein of SEQ ID NO:2 (see attached sequence alignments). Because these two proteins are so similar to the protein of SEQ ID NO: 2 of the instant invention, absent evidence to the contrary, the majority of antibodies directed to the proteins of Godbout would also specifically bind the polypeptide of SEQ ID NO: 2.

Immunobiology teaches that the antibodies generated in a natural immune response are a mixture of different antibodies (polyclonal), and also teaches Fab fragments (Fig. 3.4). Immunobiology teaches that antisera have certain disadvantages that relate to the heterogeneity of the antibodies they contain such as differences between batches, production in limited volumes, and thus it is impossible to use the identical serological reagent in a long or complex series of experiments or clinical tests. Antisera also may include antibodies that give unexpected cross-reactions. Immunobiology teaches that monoclonal antibodies can overcome these disadvantages with an unlimited supply of antibody molecules of homogeneous structure and known specificity, and such monoclonal antibodies may be made by immunizing animals and producting hybridomas (section 2-10, Fig. 2.16). Immunology also teaches that humanized

antibodies (13:8) are far less immunogenic in humans than monoclonal antibodies made in mice for example, and can be used for treatment of humans with far less risk of anaphylaxis. Immunobiology also teaches that fragments of antibodies called single-chain Fv (Fragment variable) may become valuable therapeutic agents because of their small size, allowing ready tissue penetration (page 3:4-3:5). Immunobiology also teaches that antibodies can be conjugated to a label such as a radioisotope, or antibodies can be conjugated to enzymes and used in ELISA binding assays, allowing antigen in unknown samples to be measured easily and rapidly (section 2-7, Fig. 2.6). Immunology also teaches detecting polypeptides in Western blots (Fig. 2.23), and detecting polypeptides in biological samples using antibodies (Fig. 2.14).

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to make polyclonal or monoclonal antibodies, antibody fragment or labeled antibodies to the protein of Godbout, for the reasons explained in Immunology, in order to either purify or further study the protein. The skilled artisan would be motivated to do so since the advantages of such are discussed in Immunology, and there would be a reasonable expectation of success, since making and using these antibodies have been widely and successfully used in the field of immunology.

6.2 Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over R. Godbout, Experimental Eye Research, Vol. 56, Issue 1, January 1993, pages 95-106, further in view of Immunobiology, The Immune System in Health and Disease, Third Edition, Janeway and Travers, Ed., 1997, and further in view of Sadler et al., US. Patent. No. 5,028,534.

Claim 10 is directed to isolated antibody or fragment thereof that specifically binds to a protein consisting of amino acid residues 1-132 of SEQ ID NO: 2, or 30 or 50 consecutive amino

acids of SEQ ID NO: 2, or full-length or fragment of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 97287 or 30 or 50 consecutive amino acids thereof, wherein the protein is glycosylated.

The teachings of Godbout and The Immune System in Health and Disease are discussed above. The references do not teach antibodies to glycosylated protein.

Sadler et al. teach that human proteins can be made either in eukaryotic cells, that would glycosylate proteins, or prokaryotic cells, that would not glycosylate proteins (column 3, lines 50-68).

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to produce the proteins of Godbout, for the reasons explained in Immunobiology, The Immune System in Health and Disease, in eukaryotic cells, which would likely to be glycoslyated as taught in Sadler et al., and to make antibodies against the glycosylated proteins, since these antibodies would have better binding activity to the proteins isolated from chickens than to the same proteins produced in prokaryotic cells. The skilled artisan would be motivated to do so for the reasons discussed, and there would be a reasonable expectation of success, since making and using antibodies to glycosylated proteins have been widely and successfully used in the field of immunology.

6.3 Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over R. Godbout, Experimental Eye Research, Vol. 56, Issue 1, January 1993, pages 95-106, further in view of Immunobiology, The Immune System in Health and Disease, and further in view of Hoffmann et al., US. Patent. No. 4,444,887.

Claim 11 is directed to isolated antibody or fragment thereof that specifically binds to a protein consisting of amino acid residues 1-132 of SEQ ID NO: 2, or 30 or 50 consecutive amino acids of SEQ ID NO: 2, or full-length or fragment of the polypeptide encoded by the cDNA contained in ATCC Deposit Number 97287 or 30 or 50 consecutive amino acids thereof, wherein the antibody is human.

The teachings of Godbout and Immunobilogy, The Immune System in Health and Disease are discussed above. The references do not teach antibodies which may be human.

Hoffmann teach making human antibodies using human B-lymphocytes to human antigen (see entire patent), and that this avoids that need to deal with such extraordinary pathway mitogens as the tumor producing EB virus, with their attendant dangers to personnel working with the virus and patients receiving a possibly contaminated or otherwise dangerous end product Col. 2, lines 3-20).

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to human antibodies to the protein of Godbout., for the reasons explained in Immunobiology, The Immune System in Health and Disease and in Hoffman et al., in which method of production and product obtained would be safer. The skilled artisan would be motivated to do so for the reasons discussed, and there would be a reasonable expectation of success, since making and using these antibodies have been widely and successfully used in the field of immunology.

***Conclusion***

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nichol can be reached at (571) 272-0835.

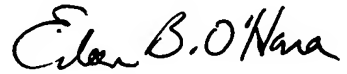
The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://portal.uspto.gov/external/portal/pair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner



EILEEN B. O'HARA
PRIMARY EXAMINER